X_1 is a cholic acid group or deoxycholic acid group; and X_2 and X_3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group, and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups;

and wherein at least one of X_2 and X_3 is a saccharide group.

40. (Amended) The method of claim 23 wherein the compound of Formula I is administered with the therapeutic agent.

REMARKS

Claims 21-22, 35-36 and 40-55 are pending in this application. Claims 21-22, 35-36 and 40 have been amended. No new matter has been introduced with the foregoing amendments. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made." The claims as pending are set forth in the Appendix for the Examiner's convenience. Reconsideration is respectfully requested.

I. The Invention

The present invention provides novel compounds and compositions that advantageously enhance the delivery of therapeutic or diagnostic agents to a cell or tissue. Included among the therapeutic and diagnostic agents that can be delivered are proteins and nucleic acids, including gene therapy vectors.

II. FIRST REJECTION UNDER 35 U.S.C. § 112, first paragraph

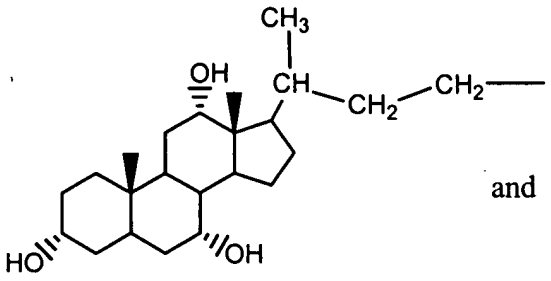
Claims 21-22, 35, 36 and 40-55 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In response, Applicants respectfully traverse the rejection.

The Examiner alleges that the specification lacks written description for the impurities in Big CHAP. The Examiner states:

> The specification and claims state X1, X2 or X3 may be a cholic acid or deoxycholic acid group. However, the specification does not teach how the cholic or deoxycholic acid groups are attached to Formula I or II. In application 09/112,074, the impurities (Fig. III-V) have three carbons between the carboxyl group and the pentose ring of the cholic acid instead of four as in cholic or deoxycholic acid (i.e. the impurities require Xl, X2 or X3 is cholic or deoxycholic acid with a deletion of the terminal O_2H). Addition of the cholic or deoxycholic acid as claimed (with the terminal O_2H) would result in four carbons between the carboxyl group and the pentose ring of the cholic or deoxycholic acid which is not the structure of the impurities disclosed in 09/112,074.

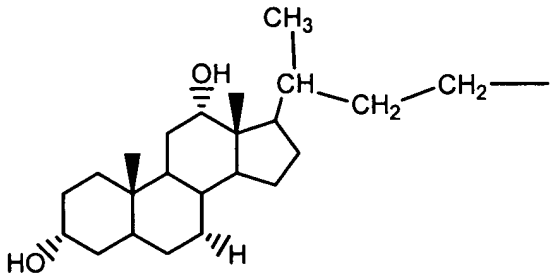
The Examiner appears to be saying that U.S. Application No. 09/112,074 discloses compounds wherein the claimed structures have 3 carbons between the carbocyclic ring and the carbonyl group, but the presently claimed structures have 4 carbons. Applicants respectfully traverse this characterization.

To remove ambiguity, the claimed terms, *i.e.*, "a cholic acid group" and "a deoxycholic acid group" have the following chemical structures:



cholic acid group

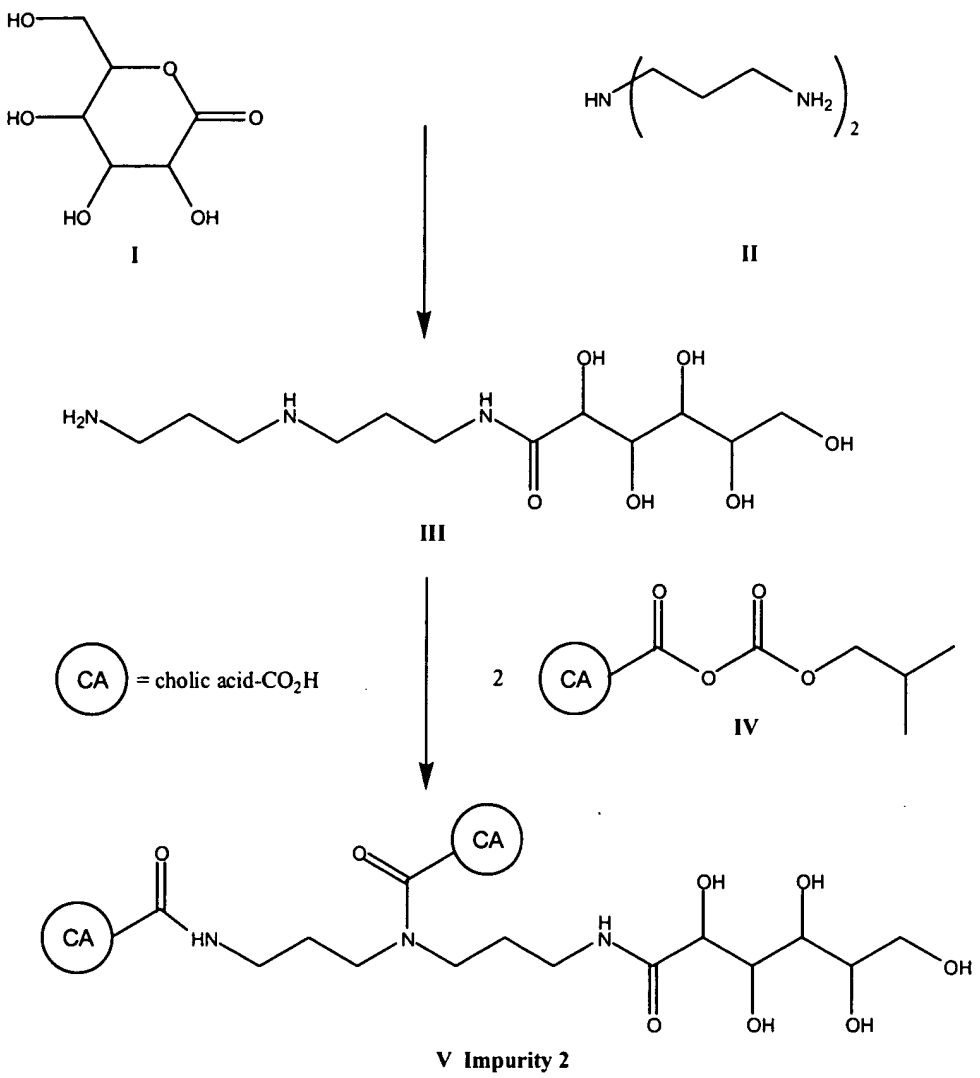
and



deoxycholic acid

As shown, the functional groups of cholic acid and deoxycholic acid have "3 carbons" in a straight chain "between the carboxyl group and the pentose ring," but "4 carbons between the carboxyl group and the pentose ring" if the branched site is included. As explained in detail directly below, it is evident that Applicants had these structures in possession when the application was filed.

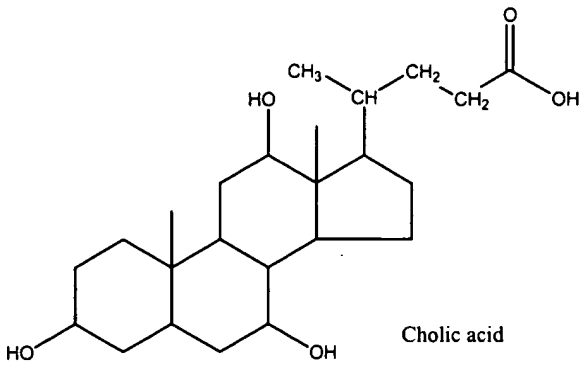
The Examiner's attention is respectfully directed to Example 12 of the present application. As described therein the following synthetic scheme is set forth:



I II III IV V Impurity 2

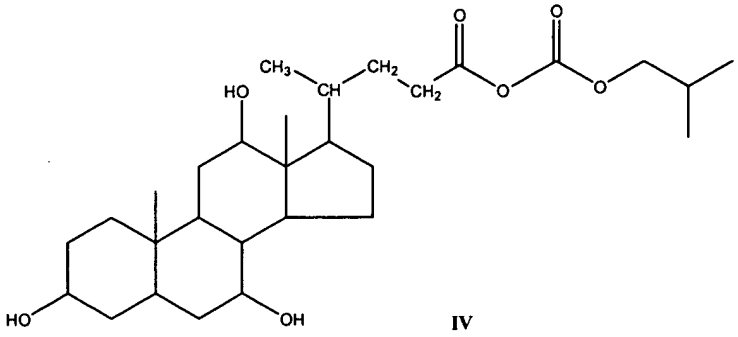
As shown above, glucono-δ-lactone I is added to iminobispropylamine II to produce 3-aminopropyl-3'-N-gluconamidopropyl-amine III. In addition, cholic acid is reacted with isobutylchloroformate which yields a mixed anhydride intermediate IV. The mixed anhydride intermediate is thereafter reacted with III to produce 3'-N-gluconamidopropyl-3''-N-cholamidopropyl-N-cholamide V (impurity 2).

Cholic acid has the following structure:



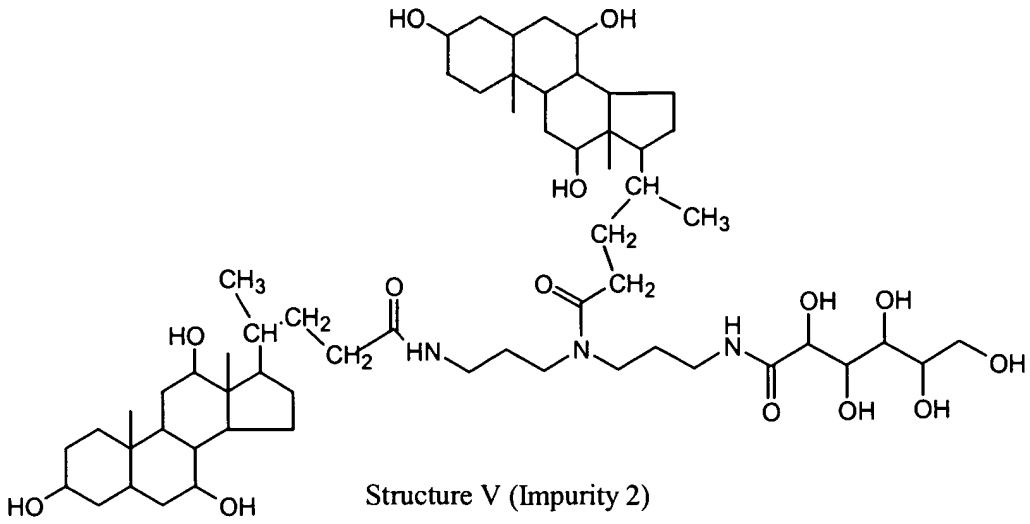
Cholic acid

When cholic acid is reacted with isobutylchloroformate as set forth in Example 12, the mixed anhydride intermediate IV is generated. A skilled person would instantly realize that structure IV is short hand notation for the following structure:



IV

Similarly, structure V is shorthand notation for the following:



Structure V (Impurity 2)

Thus, the synthetic scheme in Example 12 unambiguously leads a skilled artisan to structure V above. The synthetic scheme describing the addition of cholic acid or deoxycholic acid would appraise a skilled artisan of the proper structure. Given this detailed guidance, it is evident that the specification as filed teaches the attachment of these cholic acid groups in proper context. As such, the Examiner is urged to withdraw the rejection.

Further, Applicants are entitled to claim compounds by way of a generic formula that a skilled person would be able to make and use. If a skilled person is taught how to make representative examples of a compound such as in Example 12, it permissible to claim variations of the same.

Applicants assert that the present claims and Formula I fully comply with the requirements for written description of a chemical genus as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). The Federal Circuit reiterated that a written description for a chemical genus "requires a precise definition, such as by structure, formula, chemical name, or physical properties" (*see, University of California v. Eli Lilly & Co.*, 43 USPQ2d at 1405, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. (1995)). In addition, the Court explicitly held that description of such a genus may be achieved by "recitation of a representative number of [species] . . . or recitation of structural features common to the members of the genus" (*see, University of California v. Eli Lilly & Co.*, 43 USPQ2d at 1406.

Applicants assert that the three impurities described in the specification satisfy the requirement that there be a "recitation of a representative number of [species] . . . or recitation of structural features common to the members of the genus". Applicants isolated three impurities from Big CHAP and the results are depicted in Figure 16. Moreover, Applicants have synthesized Impurity II as set forth in Example 12. Applicants maintain that these compounds satisfy the requirement of a precise definition, such as by structure, formula, and chemical name. The specification thus appropriately describes the instantly claimed genus.

III. SECOND REJECTION UNDER 35 U.S.C. § 112, first paragraph

Claims 21, 22, 35, 36 and 40-55 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly including subject matter that was not described in the specification in such a way as to

enable one of skill in the art to make and/or use the invention. In response, Applicants respectfully traverse the rejection.

The Examiner alleges the following:

> claims 21, 22, 35, 36 and 40-55 are not enabled because Formula I (claims 21, 22, 35, 36, 40-53) and Formula II (claims 54 and 55) are not the structures of the impurities found in Big CHAP. Example 11 states three impurities (I, II and III) were isolated from Big CHAP, but the specification does not teach how the impurities were isolated or the structure of the impurities. The specification and claims state Xl, X2 or X3 in Formulas I or II are cholic or deoxycholic acid. However, the specification does not teach how the cholic or deoxycholic acid groups are attached to Formula I or II.

As discussed in detail above, the specification teaches how to make and use the claimed compounds. Example 12 is a detailed synthetic route that a person of skill could use to make compounds of Formula I. A skilled artisan would be able to make and use the claimed invention using the quantities of starting materials in grams and moles. The skilled person would be able to assess the purity of the product by using the mass spectrometry data set forth in the specification. 35 U.S.C. § 112, first paragraph requires no more. In view of this detailed guidance, Applicants respectfully request that the Examiner withdraw the rejection.

With regard the Examiner allegation that "**the specification does not teach how the impurities were isolated**", Applicants respectfully traverse this statement and direct the Examiner's attention to page 29, Example 11 of the specification as filed. As disclosed therein, thin-layer chromatography was used to isolate the impurities. The amount of solvent, the solvent ratios, and the way the TLC plates were visualized is explained in detail. As stated therein, the impurities were further isolated by column chromatography and analyzed by thin layer chromatography. The results are set forth in Figure 16. The detailed guidance is reproduced below for the Examiner's convenience.

> 2. Analysis of Big CHAP Thin Layer Chromatography:
>
> BC (Sigma or CALBIOCHEM®) was dissolved in methanol/water, 3/1, and TLC performed on Silica gel 60, 0.25 mm (EM Industries); the mobile phase consisted of:
> 1-Butanol/Water/Glacial Acetic Acid, 6/2.5/1.5. Chromatograms were visualized with 0.5g of thymol in sulfuric acid/ethanol, 5/95, and heat. As shown in Figure 15, only one distinct band developed from the sample of BC - Sigma (B), while three additional bands became evident in the sample of BC-CALBIOCHEM® (A).

> Impurities of BC (CALBIOCHEM®) were further isolated by column chromatography and analyzed by thin layer chromatography (Silica Gel 60), using a mobile phase of chloroform/methanol/water, 6/5/1. The results are depicted in Figure 16. (Lane 1: BC (CALBIOCHEM®); Lane 2: Impurity I; Lane 3: Impurity II; Lane 4: Mixture of Impurity II and III; Lane 5: Impurity III; Lane 6: BC (CALBIOCHEM®) pure; Lane 7: BC (CALBIOCHEM®)).

In view of this detailed guidance, Applicants respectfully request that the Examiner withdraw this rejection.

The Examiner further states the following:

> it appears that some of the claims are directed toward modifications of Impurities I, II or III or impurities that are different than Impurities I, II or III. The specification does not teach isolating any other impurities from Big CHAP or how to modify impurities I, II or III to obtain other compounds. Since the structure that represents Impurities I, II and III cannot be accurately determined at this time, it cannot be determined which claims are equivalent to Impurities I, II and III and which claims are modifications of Impurities I, II and III. Modifications of Impurities are not enabled because the specification does not teach how to make such compounds or how to use such compounds to deliver DNA.

Again, Applicants assert that the three impurities described in the specification satisfy the requirement that there be a "recitation of a representative number of [species] . . . or recitation of structural features common to the members of the genus". Applicants isolated three impurities from Big CHAP and the results are depicted in Figure 16. Moreover, Applicants have synthesized Impurity II as set forth in Example 12. Applicants maintain that these compounds satisfy the requirement of a precise definition, such as by structure, formula, and chemical name. The specification thus appropriately describes the instantly claimed genus.

The Examiner further alleges that

> [t]he specification does not enable one of skill to use DNA combined with Formula I as a pharmaceutic composition (claims 21 and 22) or to treat bladder cancer (claims 35, 36 and 40). **The specification does not enable one of skill to isolate or determine the structure of the impurities of BigCHAP, and Formula I does not correlate to the impurities of BigCHAP for reasons cited above.** Therefore, the

> specification does not enable using DNA combined with Formula I as a pharmaceutical composition or to treat cancer as claimed. [Emphasis added].

Applicants have provided in excruciating detail how to isolate the impurities of Big CHAP so a skilled person could isolate such impurities. Applicants have taught how to use TLC to test for the impurities. Applicants have taught how to isolate the impurities by column chromatography. Applicants have taught how to make and use the impurities. Applicants have taught how to synthesize the impurities from known starting materials available from commercial sources. Applicants have taught how to test whether the impurities are pure by mass spectrometry. 35 U.S.C. § 112, first paragraph requires no more. As such, Applicants respectfully request that the Examiner withdraw the rejection.

In addition, the Examiner alleges the following:

> the state of the art at the time of filing was such that it was unpredictable what combination of vector, promoter, route of administration, dosage, protein of interest, level of expression, and target tissue were required to obtain a **desired therapeutic effect** (Eck, Verma, Ross and Marshall all of record). The specification discloses administering adenoviral vector encoding RB operatively linked to a promoter combined with BC BigCHAP to mice and obtaining RB expression (example 6; Fig. 9). The specification does not teach administering $1x10^8$ to $5x10^{11}$ particles/ml of an adenovirus (claims 35 and 36) comprising DNA encoding RB provides a therapeutic effect. The specification does not teach the level of RB expression obtained the level of RB expression required **to obtain a therapeutic effect** or that administration of the adenoviral vector and BC BigCHAP resulted in a therapeutic effect. [Emphasis added].

Applicants traverse these allegations. Applicants' specification provides experimental data which supports the assertion that the compounds encompassed by the claims are useful not only for enhancing delivery of DNA to cells *in vivo* to achieve a therapeutic effect, but also for delivering marker genes *in vivo*. Moreover, the specification states that such compounds are also useful for enhancing delivery of agents to cells *in vitro* (page 16, lines 24-26). As set forth in M.P.E.P. §2107.02 II:

> [i]f reasonably correlated to the particular therapeutic or pharmacological utility, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility

for a compound, composition or process.

The Examiner is requiring optimization of the therapeutic effect. This is not the test. As set forth in Example 11, Number 5, impurities II and III increased β-galatosidease gene expression in the bladder epithelium in a dose dependent manner. Moreover, it would be readily apparent to those familiar with the technological field of the invention that delivery of DNA to cells *in vitro* is useful for producing proteins, including therapeutic and other proteins, *in vitro*.

With regard to the Examiner's allegation that Claims 35, 36 and 40 are not enabled because they are missing essential element such as expression of the therapeutic protein to therapeutic levels or treating bladder cancer, Applicants respectfully traverse this rejection.

Applicants are not required to show the therapeutic levels of treating bladder cancer. Applicants have shown reasonable correlation to the particular therapeutic or pharmacological utility. Applicants' specification demonstrates enhanced expression of a therapeutic gene. For example, as stated in Example 6 (page 25), the administering an RB-expressing adenoviral vector resulted in "enhanced expression using an ethanol of Big CHAP (CALBIOCHEM®) formulation," for which results "are shown in Figure 9." Further, Example 8 (page 27) showed expression of p53 in bladder tumors when an adenoviral vector was administered in a Big CHAP-containing formulation. Moreover, Applicants' specification contains several examples demonstrating that expression of a marker gene (β-gal) is enhanced when administered using formulation that contains the compounds encompassed by Applicants' claims. The Examiner is requiring optimization. As Applicants have fulfilled the requirements of 35 U.S.C. § 112, first paragraph, Applicants respectfully request that the Examiner withdraw the rejection.

IV. REJECTION UNDER 35 U.S.C. § 112, second paragraph

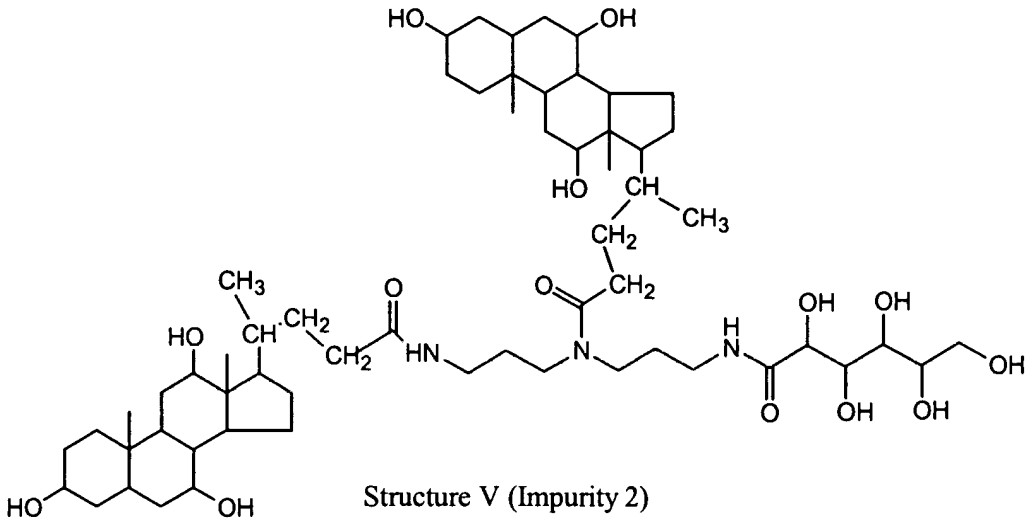
Claims 21, 22, 35, 36 and 40-55 stand rejected under 35 U.S.C. §112 second paragraph, as allegedly being indefinite. Applicants respectfully traverse the rejection.

The Examiner alleges the following:

> Example 11 states three impurities (I, II and III) were isolated from BC BigCHAP, but **the specification does not teach how the impurities were isolated or the structure of the impurities.** The claims state Xl, X2 or X3 in Formulas I or II are cholic or deoxycholic acid. However, **the specification does not teach how the cholic or deoxycholic acid groups are attached to Formula I or II.** In application 09/112,074,

> applicants disclose the structure of the impurities (Fig. III-V) which have three carbons between the carboxyl group and the pentose ring instead of four in the cholic or deoxycholic acid (i.e. the impurities require Xl, X2 or X3 is cholic or deoxycholic acid with a deletion of the terminal O_2H). Addition of the cholic or deoxycholic acid would result in four carbons between the carboxyl group and the pentose ring of the cholic or deoxycholic acid which is not the structure of the impurities of BigCHAP. Therefore, **the structures of the compounds recited in the claims are indefinite because they are not the structures of the impurities of BigCHAP disclosed in 09/112,074**. [Emphasis added].

Each of the Examiner concerns noted above will be addressed in turn. With regard to the specification teaching how the impurities were isolated or the structure of the impurities, the Examiner's attention is directed to Example 11. As disclosed therein, thin-layer chromatography was used to isolate the impurities. The amount of solvent, the solvent ratios, and the way the TLC plates were visualized is explained in detail. As stated therein, the impurities were further isolated by column chromatography and analyzed by thin layer chromatography. The results are set forth in Figure 16. This is how Applicants isolated the impurities. The structure of impurity II, for example, is set forth in Example 12. It structure is as follows:



Structure V (Impurity 2)

In view of these remarks, Applicants respectfully request that the Examiner withdraw the rejection.

With regard to the allegation that the specification does not teach how the cholic or deoxycholic acid groups is attached, the Examiner's attention is directed to the synthetic scheme set

forth above. Given this detailed guidance, it is evident how a cholic acid group or deoxycholic acid group is attached. As such, the Examiner is urged to withdraw the rejection.

With regard to the allegation that the structures of the compounds recited in the claims are indefinite because they are not the structures of the impurities of Big CHAP disclosed in 09/112,074, Applicants traverse this allegation. The impurities are the same. Applicants teach how to make Impurity II on page 31 of the specification. This is the same impurity II in U.S. Application No. 09/112,074. As such, the Examiner is respectfully requested to withdraw the rejection.

Further, claims 21, 22, 35, 36 and 40 were rejected as being indefinite because they are dependent upon claims, which have been canceled. In order to expedite prosecution of this application, Applicants have incorporated the canceled subject matter into claims 21-22, and 35-36. In view of these amendments, Applicants respectfully request that the Examiner withdraw the rejection.

Claim 40 was rejected as being indefinite because "the delivery enhancing agent" lacked antecedent basis. Applicants have amended the claim to provide the necessary antecedent basis. In view of this amendment, Applicants respectfully request that the Examiner withdraw the rejection.

In view of the foregoing, Applicants respectfully request that the Examiner withdraw all outstanding §112 rejections.

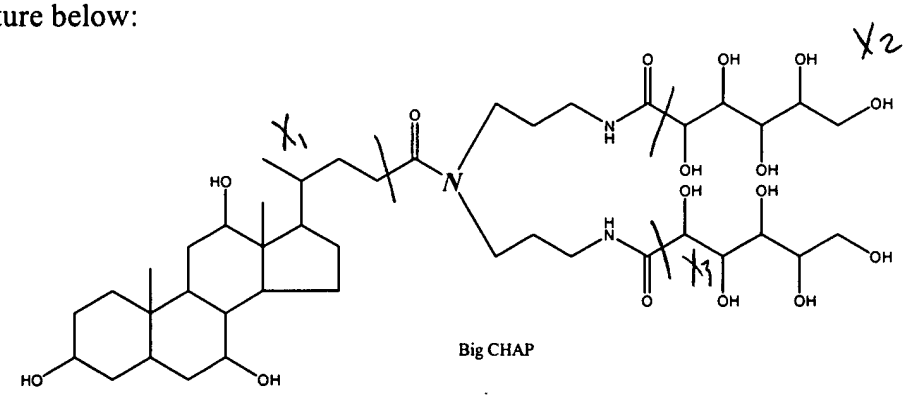
V. REJECTION UNDER 35 U.S.C. § 102(b)

Claims 41, 42, 45, 54 and 55 are rejected and claims 43, 44 and 46-53 stand rejected under 35 USC § 102(b) as allegedly being anticipated by Aungst *et al., Int. J. Pharm.*, (1993) 53: 227-235 ("Aungst *et al.*"). The cited reference discusses delivery of insulin in a formulation that includes Big CHAP. The Examiner alleges the BigCHAP is equivalent to the structure in claims 41, 42, 45 and 54.

The Examiner states:

> BigCHAP is equivalent to the structures in claims 41, 42, 45 and 54. As drawn on page 5 of applicants response, the ring structure attached to the carboxyl group on the left is equivalent to Xl and the two groups attached to the two carboxyl group on the right are equivalent to X2 and X3 which is equivalent to claims 41, 42, 45 and 55. In addition, BC BigCHAP inherently contains the Impurities I, II and III disclosed in the instant invention and the compounds in claims 43, 44 and 46-53.

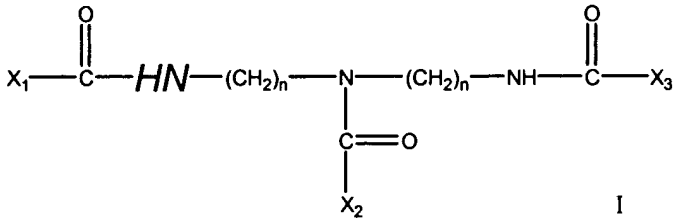
Applicants assert that the Formula I cannot read on Big CHAP. Big CHAP is N,N-Bis(3-D-gluconamidopropyl)cholamide. N,N-Bis(3-D-gluconamidopropyl)cholamide has the chemical structure below:



Big CHAP

As depicted above, Big CHAP has a chemical formula wherein the cholic acid functional group is attached to an amide bond wherein the ***nitrogen*** of the amide bond is a tertiary nitrogen (the tertiary nitrogen is enlarged and italicized in the structure above).

In contrast, the compounds of Formula I of the present invention have the following chemical formula:



I

X_1 is a is a cholic acid group or deoxycholic acid group. If X_1 is a is a cholic acid group or deoxycholic acid group, and either X_2 or X_3 is a saccharide group, it is impossible to arrive at Big CHAP with Formula I. In addition, the amide bond having a cholic acid or deoxycholic acid group appended thereto is a secondary nitrogen (bolded and italicized). This is ***not*** the same structure as Big CHAP.

Further, in certain preferred embodiments, the compounds of the instant claims have two cholic acid groups. There is simply no teaching or suggestion of two cholic acid groups in the Big CHAP compound of Aungst *et al.* Formula I does not read on Big CHAP. Therefore, Applicants respectfully request that the Examiner withdraw the anticipation rejection.

As discussed in the previous response, the Examiner's rejection based upon inherancy is misplaced. Under *In re Bergstrom*, 427 F.2d 1394, 166 USPQ 256 (CCPA 1970), *In re Cofer*, 354 F.2d 664, 148 USPQ 268 (CCPA 1966) and *In re Seaborg*, 328 F.2d 996, 140 USPQ 662 (CCPA 1964), the test becomes "whether the prior art suggests the particular structure or form of the compound or composition as well as suitable methods of obtaining that structure or form." Thus, under the applicable case law, the anticipation rejection becomes, in essence, an obviousness question. Applicants assert that nothing in the prior art teaches or suggest the compounds of Formula I. Aungst *et al.* do not teach or suggest that Big CHAP has impurities. Further, Aungst *et al.* do not teach or suggest the use of Big CHAP impurities. Aungst *et al.* do not teach or suggest a method of making the compounds of Formula I, nor do they hint at the structure of the impurities.

A compound that is purer than a previously known mixture containing the compound is patentable. Under the applicable case law, whether the prior art suggests the particular structure or form of the compound or composition is but the first step of the inquiry. The second step is whether the prior art discloses a suitable method of obtaining that structure or form. Applicants assert that Aungst *et al.* do not teach or suggest the compounds set forth in Formula I nor do they teach a method of producing it. In view of the foregoing, Applicants respectfully request that the Examiner withdraw the rejection.

VI. REJECTION UNDER 35 U.S.C. § 103

Claim 40 stands rejected under 35 USC § 103(a) as allegedly being obvious over Aungst *et al.* (*Int. J. Pharm.* (1993) 53: 227-235) in view of Carson *et al.* (U.S. Patent No. 5,804,566, issued September 8, 1998 and filed November 1, 1994). Applicants respectfully traverse the rejection.

The Examiner asserts:

> Aungst taught administering compounds to rats using BC BigCHAP (page 230, Figure 1; page 228, column 2, line 17 of Materials). **BC BigCHAP inherently contains the Impurities I, II and III disclosed in the instant invention.** As drawn on page 5 of applicants response, the ring structure of BigCHAP attached to the carboxyl group on the left is equivalent to Xl and the two groups attached to the two carboxyl group on the right are equivalent to X2 and X3 which is equivalent to claims 41, 42, 45 and 55. BigCHAP is a "delivery enhancing agent" as in claim 40. Aungst did not teach delivering DNA using BC BigCHAP. However, Carson taught delivering DNA using surfactants and

> absorption promoters (column 8, lines 55-63). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer compounds to rats using BC BigCHAP as taught by Aungst wherein the compound was DNA as taught by Carson. One of ordinary skill in the art at the time the invention was made would have recognized that BigCHAP was a surfactant and would have been motivated to add BigCHAP to DNA to improve delivery of a compound to a cell as taught by Aungst (page 230, Table 1).

The Examiner is respectfully reminded that it is improper to rely upon inherent properties in an obviousness rejection unless the inherent properties would themselves be entirely explicit to one of skill upon viewing the reference. (*see, S Kloster AB v. Crusible Inc.*, 793 F.2d 1565 (Fed. Cir. 1986)). As stated by the CCPA:

> The inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessary known. Obviousness cannot be predicated on what is unknown. *In re Shetty*, 566 F.2d 81, 195 USPQ 753, 757 (CCPA 1977).

Applicants assert that there is simply no motivation to make the modifications that the Examiner contemplates. Prior to the advent of the present invention, the structures and compounds of the instant claims were UNKNOWN. Again, the compounds of Formula I are structurally different than the structure of Big CHAP. There is absolutely no equivalence between the currently claimed compounds and the CHAP. Carson *et al.* does not supply the teaching lacking in Aungst *et al.* Carson *et al.* teach methods for introducing biologically active peptides into a host by administration of polynucleotides which operatively encode for the peptide of interest. A mammal is desensitized to an antigen, in particular an allergen, through administration to the mammal of polynucleotides, which operatively encode the antigen. The antigen-encoding polynucleotides are administered to host tissues, which have a high concentration of antigen presenting cells. There is absolutely no teaching or suggestion of N,N-Bis(3-D-gluconamidopropyl)cholamide or impurities therein.

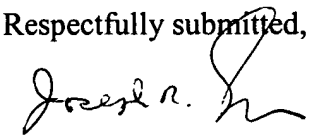
In view of the foregoing, Applicants respectfully request that the Examiner withdraw all rejections and send this application to issue.

VII. CONCLUSION

In view of the foregoing amendments and remarks, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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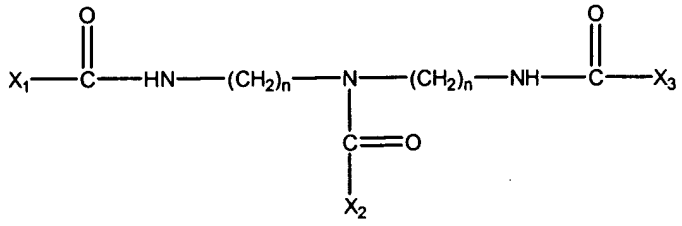
VERSION WITH MARKINGS TO SHOW CHANGES MADE

21. (Amended) [The] A pharmaceutical composition [of claim 12, wherein the composition further comprises] comprising a polymeric matrix and a therapeutically effective amount of a therapeutic agent formulated in a buffer comprising a compound of Formula I:



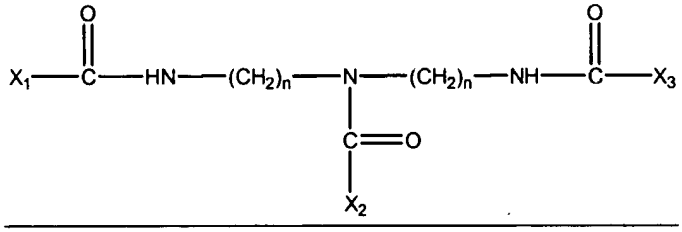
wherein:

n is an integer from 2-8;

X_1 is a cholic acid group or deoxycholic acid group; and X_2 and X_3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group, and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups;

and wherein at least one of X_2 and X_3 is a saccharide group.

22. (Amended) [The] A pharmaceutical composition [of claim 12, wherein the composition further comprises] comprising a mucoadhesive and a therapeutically effective amount of a therapeutic agent formulated in a buffer comprising a compound of Formula I:



wherein:

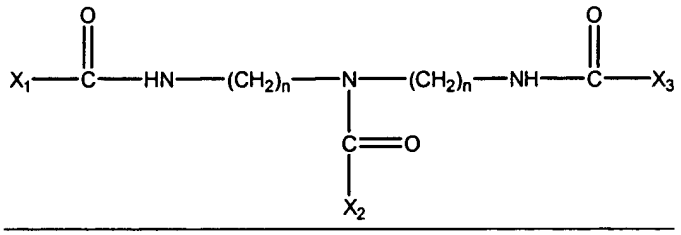
n is an integer from 2-8;

X_1 is a cholic acid group or deoxycholic acid group; and X_2 and X_3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group,

and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups;

and wherein at least one of X_2 and X_3 is a saccharide group.

35. (Amended) [The] A method of treating bladder cancer comprising administration to a cell [of claim 30] of a therapeutically effective amount of a therapeutic gene that is formulated in a buffer, wherein the therapeutically effective amount of a therapeutic gene is in the range of about from $1x10^8$ particles/ml to $5x10^{11}$-particles/ml of a recombinant adenovirus in which the therapeutic gene is inserted, comprising a compound of Formula I:



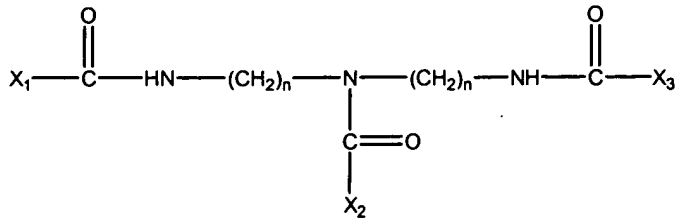
wherein:

n is an integer from 2-8;

X_1 is a cholic acid group or deoxycholic acid group; and X_2 and X_3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group, and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups;

and wherein at least one of X_2 and X_3 is a saccharide group.

36. (Amended) [The] A method of treating bladder cancer comprising administration to a cell [of claim 30] of a therapeutically effective amount of a therapeutic gene that is formulated in a buffer, wherein the therapeutically effective amount of a therapeutic gene is in the range of about from $1x10^9$ particles/ml to $5x10^{11}$-particles/ml of a recombinant adenovirus in which the therapeutic gene is inserted, comprising a compound of Formula I:



wherein:

n is an integer from 2-8;

X_1 is a cholic acid group or deoxycholic acid group; and X_2 and X_3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group, and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups;

and wherein at least one of X_2 and X_3 is a saccharide group.

40. (Amended) The method of claim 23 wherein the [delivery enhancing agent] compound of Formula I is administered with the therapeutic agent.

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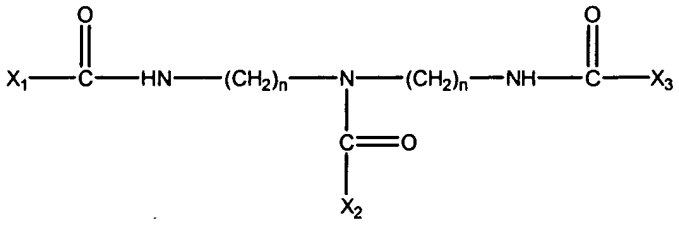
CLAIMS AS PENDING AFTER THE AMENDMENTS ARE ENTERED.

21. (Amended) A pharmaceutical composition comprising a polymeric matrix and a therapeutically effective amount of a therapeutic agent formulated in a buffer comprising a compound of Formula I:



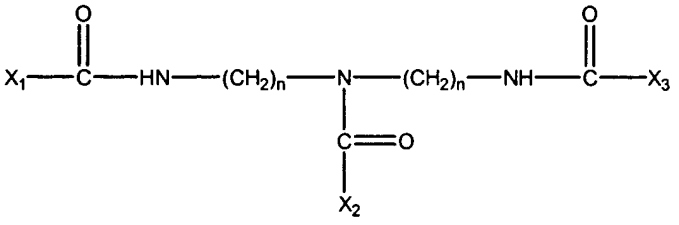
wherein:

n is an integer from 2-8;

X_1 is a cholic acid group or deoxycholic acid group; and X_2 and X_3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group, and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups;

and wherein at least one of X_2 and X_3 is a saccharide group.

1 22. (Amended) A pharmaceutical composition comprising a mucoadhisive and a
2 therapeutically effective amount of a therapeutic agent formulated in a buffer comprising a
3 compound of Formula I:



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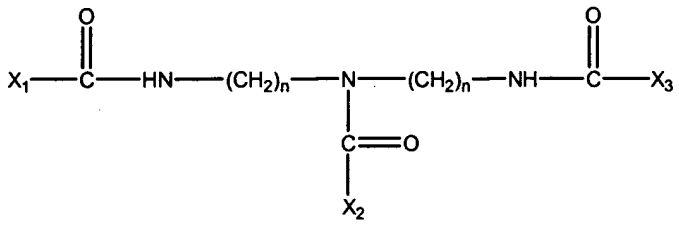
5 wherein:

6 *n* is an integer from 2-8;

X_1 is a cholic acid group or deoxycholic acid group; and X_2 and X_3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group, and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups;

and wherein at least one of X_2 and X_3 is a saccharide group.

35. (Amended) A method of treating bladder cancer comprising administration to a cell of a therapeutically effective amount of a therapeutic gene that is formulated in a buffer, wherein the therapeutically effective amount of a therapeutic gene is in the range of about from $1x10^8$ particles/ml to $5x10^{11}$-particles/ml of a recombinant adenovirus in which the therapeutic gene is inserted, comprising a compound of Formula I:



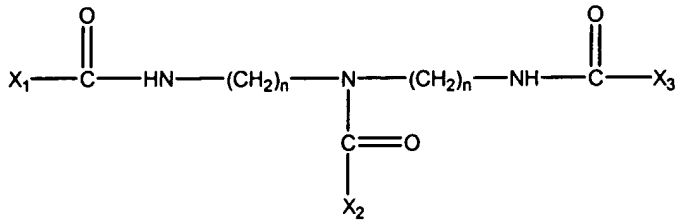
wherein:

n is an integer from 2-8;

X_1 is a cholic acid group or deoxycholic acid group; and X_2 and X_3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group, and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups;

and wherein at least one of X_2 and X_3 is a saccharide group.

36. (Amended) A method of treating bladder cancer comprising administration to a cell of a therapeutically effective amount of a therapeutic gene that is formulated in a buffer, wherein the therapeutically effective amount of a therapeutic gene is in the range of about from $1x10^9$ particles/ml to $5x10^{11}$-particles/ml of a recombinant adenovirus in which the therapeutic gene is inserted, comprising a compound of Formula I:



wherein:

n is an integer from 2-8;

X_1 is a cholic acid group or deoxycholic acid group; and X_2 and X_3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group, and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups;

and wherein at least one of X_2 and X_3 is a saccharide group.

40. (Amended) The method of claim 23 wherein the compound of Formula I is administered with the therapeutic agent.

41. A compound of Formula I:

wherein:

n is an integer from 2-8;

X_1 is a cholic acid group or deoxycholic acid group; and X_2 and X_3 are each independently selected from the group consisting of a cholic acid group, a deoxycholic acid group, and a saccharide group, wherein the saccharide group is selected from the group consisting of pentose monosaccharide groups, hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups;

and wherein at least one of X_2 and X_3 is a saccharide group.

42. The compound according to claim 41, wherein n is 3.

43. The compound according to claim 41, wherein both X_1 and X_2 are both cholic acid groups and X_3 is a saccharide.

44. The compound according to claim 41, wherein X_1 and X_2 are both deoxycholic acid groups and X_3 is a saccharide group.

45. The compound according to claim 41, wherein the saccharide group is a pentose monosaccharide group.

46. The compound according to claim 41, wherein saccharide group is a hexose monosaccharide group.

47. The compound according to claim 41, wherein the saccharide group is a hexose-hexose disaccharide group.

48. The compound according to claim 41, wherein n is 3, X_1 and X_2 are both cholic acid groups, and X_3 is a hexose monosaccharide group.

49. The compound according to claim 41, wherein n is 3, X_1 and X_3 are both cholic acid groups, and X_2 is a hexose monosaccharide group.

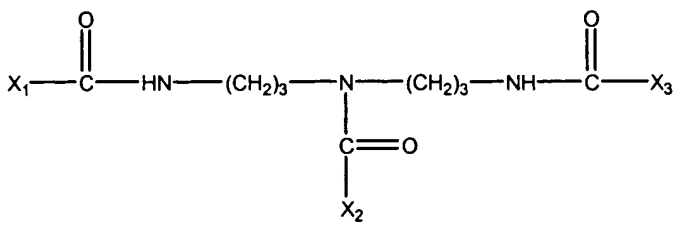
50. The compound according to claim 41, wherein n is 3, X_1 and X_2 are both cholic acid groups, and X_3 is a hexose-hexose disaccharide group.

51. The compound according to claim 41, wherein n is 3, X_1 and X_3 are both cholic acid groups, and X_2 is a hexose-hexose disaccharide group.

52. The compound according to claim 41, wherein n is 3, X_1 and X_2 are both cholic acid groups, and X_3 is a hexose-pentose disaccharide group.

53. The compound according to claim 41, wherein n is 3, X_1 and X_3 are both cholic acid groups, and X_2 is a hexose-pentose disaccharide group.

54. A compound of Formula II:



wherein:

X_1 and X_2 are each independently selected from the group consisting of a cholic acid group and a deoxycholic acid group; and

X_3 is a saccharide group is selected from the group consisting of pentose monosaccharide groups, hexose monosaccharide groups, pentose-pentose disaccharide groups, hexose-hexose disaccharide groups, pentose-hexose disaccharide groups, and hexose-pentose disaccharide groups.

55. The compound according to claim 54, wherein both X_1 and X_2 are cholic acid groups and X_3 is a glucose group.